

## Complete Summary

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### GUIDELINE TITLE

Nephropathia epidemica (NE).

### BIBLIOGRAPHIC SOURCE(S)

Makela S. Nephropathia epidemica (NE). In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2006 May 4 [various].

### GUIDELINE STATUS

This is the current release of the guideline.

This guideline updates a previous version: Finnish Medical Society Duodecim. Nephropathia epidemica (NE). In: EBM Guidelines. Evidence-Based Medicine [CD-ROM]. Helsinki, Finland: Duodecim Medical Publications Ltd.; 2004 Jun 21 [Various].

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## SCOPE

### DISEASE/CONDITION(S)

Nephropathia epidemica (NE)

### GUIDELINE CATEGORY

Diagnosis  
 Management  
 Treatment

## CLINICAL SPECIALTY

Family Practice  
Infectious Diseases  
Internal Medicine  
Nephrology

## INTENDED USERS

Health Care Providers  
Physicians

## GUIDELINE OBJECTIVE(S)

Evidence-Based Medicine Guidelines collect, summarize, and update the core clinical knowledge essential in general practice. The guidelines also describe the scientific evidence underlying the given recommendations.

## TARGET POPULATION

Patients with suspected or known nephropathia epidemica (NE)

## INTERVENTIONS AND PRACTICES CONSIDERED

### Diagnosis

1. Assessment of signs and symptoms
2. Laboratory evaluations including basic haematological parameters (haemoglobin or haematocrit, leucocyte count, and thrombocyte count), C-reactive protein, serum creatinine, and urinalysis, with chest x-ray, electrocardiogram, and ultrasonography of the kidneys, as indicated
3. Serologic testing (immunofluorescence and/or enzyme-linked immunological techniques) for antibodies to Puumala hantavirus

### Treatment/Management

1. Fluid therapy
2. Analgesics
3. Monitoring
4. Hospital care
5. Follow-up in one week to one month

## MAJOR OUTCOMES CONSIDERED

Not stated

## METHODOLOGY

## METHODS USED TO COLLECT/SELECT EVIDENCE

Hand-searches of Published Literature (Primary Sources)  
Hand-searches of Published Literature (Secondary Sources)  
Searches of Electronic Databases

#### DESCRIPTION OF METHODS USED TO COLLECT/SELECT THE EVIDENCE

The evidence reviewed was collected from the Cochrane database of systematic reviews and the Database of Abstracts of Reviews of Effectiveness (DARE). In addition, the Cochrane Library and medical journals were searched specifically for original publications.

#### NUMBER OF SOURCE DOCUMENTS

Not stated

#### METHODS USED TO ASSESS THE QUALITY AND STRENGTH OF THE EVIDENCE

Weighting According to a Rating Scheme (Scheme Given)

#### RATING SCHEME FOR THE STRENGTH OF THE EVIDENCE

Levels of Evidence

- A. Strong research-based evidence. Multiple relevant, high-quality scientific studies with homogenic results.
- B. Moderate research-based evidence. At least one relevant, high-quality study or multiple adequate studies.
- C. Limited research-based evidence. At least one adequate scientific study.
- D. No research-based evidence. Expert panel evaluation of other information.

#### METHODS USED TO ANALYZE THE EVIDENCE

Systematic Review

#### DESCRIPTION OF THE METHODS USED TO ANALYZE THE EVIDENCE

Not stated

#### METHODS USED TO FORMULATE THE RECOMMENDATIONS

Not stated

#### RATING SCHEME FOR THE STRENGTH OF THE RECOMMENDATIONS

Not applicable

#### COST ANALYSIS

A formal cost analysis was not performed and published cost analyses were not reviewed.

## METHOD OF GUIDELINE VALIDATION

Peer Review

## DESCRIPTION OF METHOD OF GUIDELINE VALIDATION

Not stated

## RECOMMENDATIONS

### MAJOR RECOMMENDATIONS

#### Essentials

- Nephropathia epidemica (NE) is an acute infectious disease in Northern Europe caused by Puumala (PUU) hantavirus (Vapalahti et al., 2003; Muranyi et al., 2005).
- The clinical picture varies from symptomless to severe.
- NE should be suspected in patients with acute febrile disease who are found to have thrombocytopenia, haematuria, and proteinureia.
- Infection confers lifelong immunity.

#### Epidemiology

- Hantaviruses are enveloped RNA-viruses found all over the world.
- In Europe and Asia, hantaviruses cause haemorrhagic fever with renal syndrome (HFRS). On the American continent, the so called hantavirus pulmonary syndrome (HPS) is encountered.
- The Puumala hantavirus is transmitted to humans by the excretions of a bank vole (*Clethrionomys glareolus*), apparently by inhalation through the airways.
- The majority of cases occur between August and January.
- NE has not been shown to transmit between humans.
- Two thirds of the patients are men.
- In children, the disease is found rather seldom and the clinical course is usually milder than in adults.

#### Clinical Picture

- The most common symptoms and signs of NE are presented in the table below:

Table. The Most Common Symptoms and Signs of NE (Mustonen et al., 1994; Lahdevirta 1971; Settergren et al., 1989)

Symptom	Frequency (%)
Fever	98–100
Headache	62–90

Symptom	Frequency (%)
Back ache	54–82
Abdominal pain	43–67
Nausea/vomiting	58–84
Myalgia	27–69
Oliguria (<400 mL/24 hours)	54–70
Polyuria (>2,000 mL/24 hours)	97
Visual disturbances	12–36
Petechiae	1–12
Diarrhoea	12–20
Cough	6–32

### Laboratory Findings

- The most common laboratory findings in NE are presented in the Table below.

Table. The Most Common Laboratory Findings in NE (Mustonen et al., 1994; Lahdevirta 1971; Settergren et al., 1989)

Finding	Frequency (%)
Proteinuria	94–100
Haematuria	58–87
Increased serum creatinine*	86–96
Thrombocytopenia	75
Increased C-reactive protein (CRP)	52–60
Increased liver enzymes	41–60
Hypoalbuminaemia/hypoproteinaemia	24–64
Leucocytosis $>10.0 \times 10^9/L$	23–57

\*Usually 3 to 7 days after the onset of fever

- In some patients, increased haemoglobin or haematocrit values are found in the acute phase; later on, anaemia is common.
- Disturbances in electrolyte balance are common but their clinical significance is usually marginal.

### Chest X-ray

- Abnormal chest x-ray findings are present in one third of hospitalized adult patients: pleural effusion, parenchymal infiltrates, and occasionally pulmonary oedema (Kanerva et al., 1996)

### Electrocardiogram (ECG)

- Nonspecific, transient changes are found in a half of the hospitalized patients: ST-depression and T-wave inversions.

### Ultrasonography of the Kidneys

- Enlarged kidneys with pleural, pericardial or perirenal effusions may be found in ultrasound examination (Paakkala et al., 2002).

### Diagnosis

- Diagnosis is based on typical clinical picture and serology.
- First-line studies in an outpatient unit include basic haematological parameters (haemoglobin or haematocrit, leucocyte count, and thrombocyte count), CRP, serum creatinine, and urinalysis.
- Antibodies to Puumala hantavirus
  - Diagnosis is confirmed with one serum sample using immunofluorescence and/or enzyme-linked immunological techniques.
  - If the result is negative and less than 6 days have elapsed since the onset of symptoms, the result should be confirmed with another sample.

### Differential Diagnosis

- Other viral infections
- Acute bacterial infections (septicaemias, pyelonephritis)
- Other types of acute nephritis

### Course of the Disease

- There are typical phases in the clinical course; however, they are not seen in all patients.
  1. Febrile phase (high fever, pains, general symptoms)
  2. Hypotensive phase (haemoconcentration, shock)
  3. Oliguric phase (renal failure, fluid retention)
  4. Polyuric phase (excessive urinary secretion)
  5. Convalescence phase (days, weeks, or even months)
- About 5% of hospitalized patients need dialysis.
- Severe course of the disease is associated with HLA-B8 and DR3 (Mustonen et al., 1996).

### Treatment

- Mild cases may be treated in primary health care on an outpatient basis or on the observation ward of a health centre.
  - Fluid therapy
  - Analgesics
    - Paracetamol is a suitable analgesic; non-steroidal anti-inflammatory drugs (NSAIDs) should be avoided because they impair renal function.
  - Patient's condition and laboratory parameters should be frequently monitored: depending on the clinical picture, the situation is assessed every 2 or 3 days or even daily if necessary.
- Indications for referral to for hospital care
  - Deteriorated general condition
  - Dehydration
  - Fluid retention
  - Renal failure (serum creatinine >150 micromol/L), oliguria

- Uncertain diagnosis

#### Follow-up

- A control visit is recommended one week to one month after hospital discharge depending on the severity of the disease, especially if acute renal failure was associated with NE. The clinical condition and the laboratory parameters should be normalized one month after the onset of the disease.
- Fatigue may continue several weeks after the acute phase.

#### Prognosis

- Mortality with NE is low (<0.1%).
- Long-term prognosis with the disease is good (Miettinen et al., 2006).
- Panhypopituitarism and chronic glomerulonephritis have been described as rare long-term complications of NE.

#### Prevention

- There is no research evidence on the possible benefit from a respirator mask in the prevention of NE.
- For the time being, there is no vaccine against the Puumala virus.

#### CLINICAL ALGORITHM(S)

None provided

### EVIDENCE SUPPORTING THE RECOMMENDATIONS

#### REFERENCES SUPPORTING THE RECOMMENDATIONS

[References open in a new window](#)

#### TYPE OF EVIDENCE SUPPORTING THE RECOMMENDATIONS

Concise summaries of scientific evidence attached to the individual guidelines are the unique feature of the Evidence-Based Medicine Guidelines. The evidence summaries allow the clinician to judge how well-founded the treatment recommendations are. The type of supporting evidence is identified and graded for select recommendations (see the "Major Recommendations" field).

### BENEFITS/HARMS OF IMPLEMENTING THE GUIDELINE RECOMMENDATIONS

#### POTENTIAL BENEFITS

Accurate diagnosis and appropriate management/treatment of nephropathies epidemica (NE)

#### POTENTIAL HARMS

Not stated

## CONTRAINDICATIONS

### CONTRAINDICATIONS

Non-steroidal anti-inflammatory drugs should be avoided with nephropathies epidemica (NE) because they impair renal function.

## IMPLEMENTATION OF THE GUIDELINE

### DESCRIPTION OF IMPLEMENTATION STRATEGY

An implementation strategy was not provided.

## INSTITUTE OF MEDICINE (IOM) NATIONAL HEALTHCARE QUALITY REPORT CATEGORIES

### IOM CARE NEED

Getting Better

### IOM DOMAIN

Effectiveness

## IDENTIFYING INFORMATION AND AVAILABILITY

### BIBLIOGRAPHIC SOURCE(S)

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### ADAPTATION

Not applicable: The guideline was not adapted from another source.

### DATE RELEASED

2004 Jun 21 (revised 2006 May 4)

### GUIDELINE DEVELOPER(S)

Finnish Medical Society Duodecim - Professional Association

### SOURCE(S) OF FUNDING



Finnish Medical Society Duodecim

## GUIDELINE COMMITTEE

Editorial Team of EBM Guidelines

## COMPOSITION OF GROUP THAT AUTHORED THE GUIDELINE

Primary Author: Satu Makela

## FINANCIAL DISCLOSURES/CONFLICTS OF INTEREST

Not stated

## GUIDELINE STATUS

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## GUIDELINE AVAILABILITY

This guideline is included in a CD-ROM titled "EBM Guidelines. Evidence-Based Medicine" available from Duodecim Medical Publications, Ltd, PO Box 713, 00101 Helsinki, Finland; e-mail: [info@ebm-guidelines.com](mailto:info@ebm-guidelines.com); Web site: [www.ebm-guidelines.com](http://www.ebm-guidelines.com).

## AVAILABILITY OF COMPANION DOCUMENTS

None available

## PATIENT RESOURCES

None available

## NGC STATUS

This NGC summary was completed by ECRI on August 30, 2005. This NGC summary was updated by ECRI on August 7, 2006.

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